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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/698,597 | 10/31/2003 | Leonard G. Presta | 39766-0033CP2C2-C1 | 1656 |

25213 7590 03/08/2007
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| EXAMINER |
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DAVIS, MINH TAM B

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| ART UNIT | PAPER NUMBER |
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1642

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
|--|------------|---------------|
| 3 MONTHS | 03/08/2007 | PAPER |

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

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|------------------------------|------------------------|--|---------------------|--|
| Office Action Summary | Application No. | | Applicant(s) | |
| | 10/698,597 | | PRESTA ET AL. | |
| | Examiner | | Art Unit | |
| | MINH-TAM DAVIS | | 1642 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 December 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 6-12 is/are pending in the application.
- 4a) Of the above claim(s) 10 and 11 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 6-9, 12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date <u>12/01/06</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Accordingly, claims 6-9, 12 are examined in the instant application.

Election/Restrictions

The restriction requirement of 10/24/06 is still deemed to be proper, and therefore made FINAL.

Information Disclosure Statement

The references in the Information Disclosure Statement of 12/01/06 have been reviewed, and a signed PTO-1449 is enclosed therehere.

Priority Date

It is acknowledged that the priority date of claims 6-9, 12 of the instant application SN=10/698597 is 03/18/1994, the filing date of the parent application SN= 08/215,139.

Specification

The amendment of the specification in the response of 12/01/06 is acknowledged.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-9, 12 remain rejected under 112, first paragraph, for lack of a clear written description of “a neurotrophic factor”, “human trkB receptor polypeptide”, and “NT-4 or NT-4/5”, for reasons already of record in paper of 10/24/06.

The response recites the case law Falkner v. Inglis and asserting that the Federal Circuit stated that Lilly does not set forth a per se rule that whenever a claim limitation is directed to a macromolecule, the specification must always recite the gene or sequence, and that where accessible literature source clearly provided genes and their nucleotide sequences, the written description requirement does not require either the recitation or incorporation by reference of such genes or sequence.

The response has been considered but is not found to be persuasive for the following reasons:

The case law Falkner v. Inglis does not apply in the instant application because the claimed neurotrophic factor, human trkB receptor, or NT-4 or NT-4/5 encompass a genus of numerous variant neurotrophic factor and human trkB receptor, or NT-4 or NT-4/5, the structure of which genus of variants is **not disclosed** in the specification, nor **in the art**, and cannot be predicted.

The claimed neurotrophic factor, human trkB receptor, or NT-4 or NT-4/5 does not meet the standards as shown by Lilly or Enzo, because the recited single human trkB receptor SEQ ID

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NO:2, and its truncated intracellular domain, SEQ ID NO:40 are not representative species to support the broad breath of the claimed genus, and because there is no disclosed functional characteristics coupled with a known or disclosed correlation between structure and function. Thus one would conclude that Applicant did not have possession of the claimed neurotrophic factor, human trB receptor, or NT-4 or NT-4/5 at the time the invention was made. Since the specification and the claims fail to describe the product for use in the claimed method, they also fail to adequately describe the claimed method.

Concerning the requirement for the recitation in the specification the essential materials, the sequences of NT-4 or NT-4/5, which are however only incorporated by references, as per MPEP 608.01, the rejection is under 112, first paragraph, enablement and is not under the written description rejection, and thus the argument citing Lilly in Falkner v. Inglis is moot here. Further, the cited passage of the case law Falkner v. Inglis does not address the issue of essential materials, that are however only incorporated by reference.

Claim Rejections - 35 USC § 112, First Paragraph, Enablement

A. Claims 6-9, 12 remain rejected under 112, first paragraph, for lack of enablement for a method of diagnosis of any pathological condition, any malignancy, any tumor or any pancreatic disorder that over- or underexpresses a neurotrophic factor, or NT-4 or NT-4/5, for reasons already of record in paper of 10/24/06.

The following are the analysis of the *Wands* factors :

1) The nature of the invention

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The response asserts that the nature of the claimed invention is routine in the art, requiring contacting and detecting over- or under-expression of a neurotrophic factor.

The response has been considered but is not found to be persuasive for the following reasons:

Contrary to the assertion, the claimed method is not routine, encompassing a method for diagnosing any pathological conditions, including any malignancy, any tumor or abnormal growths, or any pancreatic disease that over- or underexpresses a neurotrophic factor, or NT-4 or NT-4/5. However, there is no correlation between the claimed over- or underexpression of a neurotrophic factor, or NT-4, or NT-4/5 and a pathological condition, including any malignancy, any tumor or abnormal growths, or any pancreatic disease. Which pathological condition, which malignancy, which tumor or which pancreatic disease under- or over-expresses the claimed neurotrophic factor, or NT-4 or NT-4/5 is not predictable, nor disclosed in the specification, or in the art, other than the underexpression of NT-4 in pancreatic cancer, disclosed by Schneider et al, 2001.

2) The state of the prior art.

The response asserts that as acknowledged by the Examiner, the closest prior art fails to teach detection of NT-4 using human trkB receptor.

The Examiner takes note that although the closest art, Schneider et al, 2001, of record, does not teach using human trkB receptor to detect NT-4 in pancreatic cancer, the art teaches detecting of under-expression of NT-4 in pancreatic cancer, using an anti-NT-4 antibody.

3) The relative skill of those in the art

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The response asserts that the relative skill in the art is high, and it would not be undue experimentation for one of skill in the art to practice the claimed invention, because detection of labeled polypeptide is well-known and routine in the art..

The response has been considered but is not found to be persuasive for the following reasons:

Although method of detection of labeled polypeptide is known in the art, it would be undue experimentation for one of skill in the art to practice the claimed invention, because one cannot predict that the claimed neurotrophic factor is over- or underexpressed in a pathological condition, such as any malignancy, any abnormal growth, or any pancreatic disorder.

4) The unpredictability of the art

The response asserts that the issue of binding or expression of the neurotrophic factor is moot, because the claims only refer to those conditions wherein neurotrophic factors and receptors are over- or under-expressed, and where the neurotrophic factors are capable of binding to the receptors.

The response has been considered but is not found to be persuasive for the following reasons:

Which pathological conditions, which malignancy, which tumor or which pancreatic disease under- or over-expresses the claimed neurotrophic factor , or NT-4 or NT-4/5 is not predictable, other than the underexpression of NT-4 in pancreatic cancer, disclosed by Schneider et al, 2001, because the level of expression of a protein, such as TrkB or trkA or TrkC, in a disease is unpredictable, in view of the teaching of Soontornniyoomkij et al and Guate et al, all of record . Soontornniyomkij et al, 1999 (Acta neuropathologica 98(4): 345-8) teach that

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expression of trkB proteins is characteristic of particular disease processes, as shown by the absence of BDNF and trkB protein in glia cells in AD patients, in contrast to their presence in HIV patients (abstract, last seven lines). Similarly, Guate et al, 1999 (BJU Internatl, 84: 495-502) teach that trkA and TrkC are overexpressed in prostate cancer, as compared to normal prostate tissue, while trkB is not detected in prostate cancer (abstract, p.496, second column, last paragraph).

Moreover, one cannot predict that the claimed genus of variant trkB receptor with unknown structure and the claimed genus of variant neurotrophic factor, or variant NT-4 or NT-4/5 with unknown structure would have the configuration necessary for their binding to each other, in view of the teaching of Bowie, Burgess et al, and Lazar et al, all of record, because both the ligand and the receptor have to have a certain molecular configuration specificity, like lock and key, for their specific binding. Further, one cannot predict that the claimed method would be specific for NT-4 or NT-4/5, because one cannot predict that NT-4 or NT-4/5 is the only ligand for the trkB receptor.

5) The breadth of the claims

The response asserts that the claims are limited to the pathological conditions to be diagnosed be one that is characterized by the over- or undeexpression of a neurotrophic factor.

The response has been considered but is not found to be persuasive for the following reasons:

The claims are broad, because they encompass diagnosis of a genus of numerous possible pathological conditions, or malignancy, or tumor or pancreatic disorder that under- or overexpresses a genus of variant neurotrophic factor, or variant NT-4, or NT-4/5.

6) The amount of direction and the absence of working example.

The response asserts that there is no limitation in the claims that the neurotrophin does not exist in the corresponding control sample. The response asserts that moreover, the specification and the literature cited therein disclose that the human trkB receptor bind neurotrophic factors such as NT-4 or NT-4/5, and teach tissue distributions of such receptors. The response asserts that the disclosed methods and techniques enable one to practice the claimed invention by directing that person to a pathological condition of those tissues and conditions.

The response has been considered but is not found to be persuasive for the following reasons:

Although the specification discloses that the human trkB receptor bind neurotrophic factors such as NT-4 or NT-4/5, and teach distributions of such receptors in normal tissues, the specification does not teach which diseased tissue or which disease under- or overexpresses the claimed neurotrophic factor, as compared to the normal corresponding control.

Given the above unpredictability, and in view of the complex nature of the invention, a lack of sufficient disclosure in the specification, and little is known in the art concerning the claimed invention, it would have been undue experimentation for one of skill in the art to practice the claimed invention.

B. Claims 6-9, 12 are also rejected under 112, first paragraph, because the cited NT-4 or NT-4/5 are **essential materials** for the claimed method, which are however only incorporated by reference to publication in the art, in view of the teaching of MPEP 608.01, for reasons already of record in paper of 10/24/06.

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Rejection remains, because the response does not address the issue of lack of enablement, due to incorporating the essential material by reference to a publication, in view of the teaching of MPEP 608.01. The cited passage of the case law Falkner v. Inglis under written description section, supra, does not address the issue of essential materials, that are however only incorporated by reference.

NEW REJECTION BASED ON THE AMENDMENT

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-9, 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6-9, 12 are indefinite, because it is not clear in claim 6 the over- or underexpression of a neurotrophic factor is as compared to what.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SHANON FOLEY can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MINH TAM DAVIS

February 16, 2007


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